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PATENT  
Attorney Docket No.: KNAUTHE-09734

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Gabriele Multhoff  
Serial No.: 10/526,586  
Filed: 12/12/2005  
Entitled: **Use of Granzyme B as an HSP70/HSP70 Peptide Dependent Inducer of Apoptosis in Tumor Cells**

Group No.: 1615  
Examiner:

**REQUEST FOR CORRECTION OF  
FILING RECEIPT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

**CERTIFICATE OF MAILING UNDER 37 CFR § 1.8(a)(1)(i)(A)**

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Date: February 9, 2006

By: \_\_\_\_\_

  
Jasmine M. Stansberry

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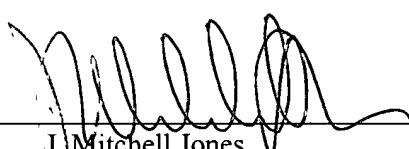
The information shown on the attached Filing Receipt contains an error:

1. The Filing Receipt currently lists the title "Use Of Granme B As An HSP70/HSP70 Peptide Dependent Inducer Of Apoptosis In Tumor Cells". The correct title should be "Use of Granzyme B As An HSP70/HSP70 Peptide Dependent Inducer Of Apoptosis In Tumor Cells". (See attached copy of first page of Specification of Application and Incorrect Filing Receipt).

Applicant(s) hereby request(s) that the Filing Receipt be corrected accordingly.

Respectfully submitted,

Date: February 9, 2006

  
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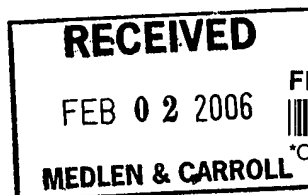
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APPL NO.	FILING OR 371 (c) DATE	ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO	DRAWINGS	TOT CLMS	IND CLMS
10/526,586	12/12/2005	1615	1195	KNAUTHE-09734	9	24	5

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CONFIRMATION NO. 3810

FILING RECEIPT



\*O000000017939176\*

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Receipt is acknowledged of this regular Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please mail to the Commissioner for Patents P.O. Box 1450 Alexandria Va 22313-1450. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).**

**Applicant(s)**

Gabriele Multhoff, Munchen, GERMANY;

**Power of Attorney:**

John Jones-44174

**Domestic Priority data as claimed by applicant**

This application is a 371 of PCT/EP03/09341 08/22/2003

**Foreign Applications**

EUROPEAN PATENT OFFICE (EPO) 020182846 08/23/2002

**Projected Publication Date:** 05/11/2006**Non-Publication Request:** No**Early Publication Request:** No**\*\* SMALL ENTITY \*\*****Title**

PRIOR ART STATEMENT DUE 3 MONTHS 5/23/05  
FOREIGN FILING LETTER DUE \_\_\_\_\_  
6 MONTHS UTILITY / 3 MONTHS DESIGN \_\_\_\_\_  
FOREIGN FILING DEADLINE \_\_\_\_\_  
12 MONTHS UTILITY / 6 MONTHS DESIGN \_\_\_\_\_  
TWENTY-ONE MONTHS SUSPENSE DATE 11/23/06  
*210*

Should be  
"granzyme"

Use of granme b as an hsp70/hsp70 peptide dependent inducer of apoptosis in tumor cells

## Preliminary Class

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Use of granzyme B as an Hsp70/Hsp70 peptide dependent  
inducer of apoptosis in tumor cells

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10 The present invention relates to a method of inducing or enhancing the expression  
of granzyme B in natural killer (NK) cells. The present invention relates also to a  
use of said NK cells for the preparation of a pharmaceutical composition for the  
treatment of tumors, viral or bacterial infections or inflammatory diseases. Further,  
the present invention relates to the use of granzyme B for the treatment of tumors,  
viral or bacterial infections or inflammatory diseases, wherein the tumor cells or the  
15 cells affected by said infection or inflammation express Hsp70 on their cell surface.

A variety of documents is cited throughout this specification. The disclosure  
content of said documents is herewith incorporated by reference.

20 Elevated cytoplasmic levels of heat shock protein 70 (Hsp70) have been found to  
protect tumor cells against programmed cell death (Nylandsted et. al. (2000) Ann.  
N.Y. Acad. Sci. 926, 122). Hsp70 is the major stress inducible form of the heat  
shock protein family (HSP), which is primarily located in the cytosol. Evidence  
accumulated during recent years has demonstrated that extracellular localized and  
25 plasma membrane-bound HSPs are highly immunogenic and expose the cells to  
immune attack (Schild et. al. (1999) Current Opinion in Immunology 11, 109).  
Following receptor-mediated uptake (Arnold-Schild et. al. (1999) J. Immunol. 162,  
3757) and re-presentation by antigen presenting cells (APC), HSP-chaperoned  
peptides elicit a cytotoxic, CD8<sup>+</sup> T cell response (Suto et. al. (1995) *Science* 269,  
30 1585). Several receptors, including CD91 and toll-like receptors 2 and 4 (TLR2/4),